REMARKS

The Specification

The specification has been amended to specify that PCT/CA99/00844 is a continuation-in-part application of U.S. Application Serial No. 09/154,627 (now abandoned).

Applicants respectfully submit that these amendments do not constitute new matter and respectfully request entry thereof.

The Claims

Claims 1-7 are currently pending in this application. Claims 1 and 2 have been amended. Claims 6-7 have been withdrawn from consideration. No new matter is being hereby introduced.

Claims 1-2 have been amended to delete non-elected SEQ ID NO: 12, as requested by the Examiner.

Claim 2 has been amended to replace the phrase "at least about 90% homology" with the phrase "at least about 75% homology" since two amino acids changed in an eight amino acid peptide gives peptides 75% homologous to the native peptide. Applicants demonstrate with 10 peptides which differ by at most 2 amino acids and retains the desired activity. Accordingly, the applicants support various peptides having 75% homology and which retain F2 receptor and prostaglandin antagonism.

Support for additional claim 10 may be found in the instant specification at page 5, lines 24-33, where administration of antagonist reducing uterine contraction.

Applicants respectfully submit that these amendments do not constitute new matter and respectfully request entry thereof.

Double Patenting

Applicants acknowledge the withdrawal of the rejection of claims 1-5 under the judicially created doctrine of obviousness-type double patenting in view of Applicants' previous arguments that SEQ ID NOs: 1 and 4-11 are not described, nor suggested, in U.S. Patent 6,300,312.

Claim Rejections – 35 U.S.C. §112, first paragraph- enablement

Claims 1-5 stand rejected under 35 U.S.C. 112, first paragraph, on the grounds that the specification, while being enabling for the peptides of SEQ ID NO:1 and 4-11, does not reasonably provide enablement for proteins which are "at least 90% homologous" to these SEQ ID NOs, nor does the specification provide enablement for "preventing" premature delivery of a fetus, or dysmenorrhea. It is the Examiner's position that the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Applicants note that as the Examiner has pointed out, "even one change in these peptides would produce a protein which is approximately 88% identical to SEQ ID NOs: 1 and 4-11". Claim 2 has been amended to substitute the phrase "at least about 90% homology" with the phrase "at least about 75% homology" since two amino acids changed in a 8 amino acid peptide provides peptides with 75% homology to the native peptide. Claim 2 as amended now address the Examiner's concerns regarding claiming all peptides having an amino acid sequence that is at least 75% homologous to SEQ ID NOs: 1 and 4-11. Regarding a functional limitation to claim 2, "wherein said peptide is a prostaglandin F2 receptor antagonist" has been added as suggested by the Examiner. Therefore, the Examiner's contention that the breadth of claims is excessive is believed to have been overcome by such amendments.

Furthermore, applicants respectfully disagree with the Examiner's contention that there is no correlation between uterine contractions and successful prevention of premature delivery of a fetus *in vivo* or of preventing dysmenorrhea. The Examiner's attention is respectfully directed to the instant specification at page 1, line 31 – page 2, line 31 which recites that prostaglandins initiate labor and increase uterine contractility. The Examiner's attention is respectfully directed to The Pharmacological Basis of Therapeutics (Eds. Louis S. Goodman and Alfred Gilman, Fifth Edition, Macmillan Publishing Co., Inc., New York, ©1975, pp. 644-647) which provides an overview of prostaglandins and smooth muscle, particularly the uterus. Specifically, "the human uterus *in vivo*, whether pregnant or not, is always contracted by PGE1, PGE2, and

PGF2α administered intravenously. The response is prompt and dose dependent...Intravenous infusion results in sustained labor-like contractions...." This reference indicates that administration of prostaglandins results in labor-like uterine contractions. Additionally, the correlation between FP receptor antagonists and pre-term labor is reported in an article co-authored by the inventors of the present invention, Sylvain Chemtob and Krishna G. Peri, which provides a pre-term labor mouse model (Peri, et al. Seminars in Perinatology 26:389-397, 2002). The endotoxin-induced pre-term mouse model was used to test the effects of the FP receptor antagonist, such as, THG113. This article reports the effects of a prostaglandin F2α antagonist in delaying pre-term labor, as well as the effectiveness of the antagonist in preventing premature delivery of the fetus. The Examiner's attention is respectfully directed to pages 394-395 where Figure 6 A clearly shows that the FP receptor antagonist delayed delivery of the mouse pups such that two-thirds of the animals still had not been delivered 24 hours after LPS treatment. Therefore, applicants respectfully submit that a method for the prevention of premature delivery or pre-term labor is evidenced by the instant specification as well as by the above-mentioned article.

Claim 4 stands rejected for lack of evidence relating dysmenorrhea to uterine contractions. However, applicants respectfully direct the Examiner's attention to the instant specification at page 1, line 31 – page 2, line 31 where an increase in prostaglandin levels, such as $PGF_{2\alpha}$ levels, results in myometrial spasms which underlie the pathogenesis of dysmenorrhea. Further, at page 16, Example 4, the FP receptor antagonists or PCP peptides prevent *ex vivo* basal contraction in porcine uterine tissue in a dose-dependent manner and at page 17, Example 5, the PCP peptides reverse the basal tone or contractile state of the uterine muscle when the change in basal levels of average tension is measured. (*See*, Figs. 3 and 4, respectively). Applicants respectfully direct the Examiner's attention to Exhibit II, an excerpt from the commonly known and accepted Merck Manual (Ed. Mark H. Beers, Robert Berkow, and Mark Burs; Merck & Co., Inc. Whitehouse Station, NJ), which correlates dysmenorrhea and uterine contractions.

Therefore, in view of the aforementioned reasons, the instant specification demonstrates that the claimed antagonists are successful in preventing premature delivery

of a fetus and in preventing dysmenorrhea. Applicants respectfully disagree with the Examiner's assertion that the term "Prevention implies that 100% of a target population would be 100% free from any of the claimed disorders." The term "prevent" is defined by Webster's Third International Dictionary of the English Language Unabridged (Editor-in-Chief, Philip Babcock Gove, Merriam-Webster, Inc. Springfield, MA © 1993), as "to keep from happening or existing especially by precautionary measures: hinder the progress, appearance or fulfillment of" and "to hold or keep back: hinder, stop." Therefore, applicants believe that one skilled in the art would understand how to use the claims directed to methods of prevention from reading the instant specification and/or commonly understood knowledge in the art. The Examiner's argument regarding 100% prevention is contrary to the law. *See*, Scott v. Finney ((CA FC) 32 USPQ2d 1115), where "testing need not show utility beyond a possibility of failure, but only utility beyond a probability of failure. Taylor v. Swingle , 136 F.2d 914, 917, 58 USPQ 468, 471 (CCPA 1943)". If a drug was successful in preventing 20% of all cancer, one would be providing a very valuable benefit to cancer patients.

Applicants respectfully submit that the rejection to claims 1-5 under 35 U.S.C. §112, first paragraph has been overcome and respectfully request reconsideration and withdrawal of this rejection to the claims on this ground.

Claim Rejections – 35 U.S.C. §112, second paragraph

Applicants understand that the rejection of claims 1 and 3-5 under 35 U.S.C. §112, second paragraph has been withdrawn.

Claim 2 stands rejected under 35 U.S.C. 112, second paragraph, on the grounds that the metes and bounds of "at least about 90% homology" are not known. Applicants respectfully traverse the rejection. Applicants note that Claim 2 has been amended herein and is directed to a peptide selected from amino acid sequences of SEQ ID NOs: 1 and 4-11.

Furthermore, with respect to the Examiner's contention that the claim is indefinite because it is not understood as to what is meant by the phrase "D-amino acid, an amino acid sequence," applicants have amended the claim to recite "D-amino acids, and an

amino acid sequence." One skilled in the art understands that L-amino acids and D-amino acids are simply different isomeric conformations (*See*, page 5, lines 11-17).

Applicants respectfully submit that this 35 U.S.C. §112, second paragraph rejection has been overcome and respectfully request reconsideration and withdrawal of the rejection to the claims on this ground.

In view of the above, it is respectfully solicited that the Examiner's rejection of claims 1 - 5 be reconsidered and withdrawn.

It is submitted, therefore, that claims 1 – 5 are in condition for allowance. Reconsideration of the Examiner's rejections is respectfully requested. Allowance of claims 1 - 5 at an early date is respectfully solicited.

AUTHORIZATION

No additional fees are believed to be necessitated by this amendment. However, should this be an error, authorization is hereby given to charge Deposit Account No. 13-4500, Order No. 2861-4003 for any underpayment or to credit any overpayment.

In the event that there are any questions concerning this amendment or the application in general, the Examiner is respectfully urged to telephone the undersigned so that prosecution of this application may be expedited.

Respectfully submitted,
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